



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/686158/2014  
EMA/H/C/000610

## EPAR summary for the public

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# Noxafil

## posaconazole

This document is a summary of the European public assessment report (EPAR) for Noxafil. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Noxafil.

### What is Noxafil?

Noxafil is an antifungal medicine that contains the active substance posaconazole; it is available as an oral suspension (40 mg/ml), a concentrate (300 mg) for solution for infusion (drip) into a vein and as gastroresistant tablets (100 mg). Gastroresistant means that the tablets pass through the stomach without being broken down until they reach the intestine.

### What is Noxafil used for?

Noxafil is used to treat adults (aged 18 years or over) with the following fungal diseases, when treatments with other antifungal medicines (amphotericin B, itraconazole or fluconazole) cannot be tolerated or have failed:

- invasive aspergillosis (fungal infection caused by *Aspergillus*),
- fusariosis (fungal infection caused by *Fusarium*),
- chromoblastomycosis and mycetoma (long-term fungal infections of the skin or the tissue just below the skin, usually caused by fungal spores infecting wounds due to thorns or splinters),
- coccidioidomycosis (fungal infection of the lungs caused by breathing in spores).

Noxafil oral suspension is also used as a first-line treatment for 'thrush', a fungal infection of the mouth and throat due to *Candida*. It is used in patients whose infection is severe or patients with weakened immune systems, when medicines applied topically (directly on the thrush) are unlikely to work.



Noxafil oral suspension, solution for infusion and gastro-resistant tablets are also used to prevent invasive fungal infections in patients whose immune system is weakened because of treatments they are receiving for blood or bone marrow cancers or medicines used in haematopoietic stem cell transplantation (a transplant of cells that make blood cells).

The medicine can only be obtained with a prescription.

## How is Noxafil used?

Noxafil treatment should be started by a doctor who has experience in managing fungal infections or in treating patients at high risk of invasive fungal infections.

Noxafil oral suspension and tablets have different dosages and should not be used interchangeably.

- Noxafil tablets can be taken with or without food and should be swallowed whole with water; the tablets should not be crushed, chewed, broken or dissolved.
- Noxafil oral suspension is taken with a meal or nutritional supplement; the suspension must be shaken well before use.

For the treatment of fungal infections, with the exception of oral candidiasis, Noxafil oral suspension is taken at a dose of 400 mg (10 ml) twice a day, or 200 mg (5 ml) four times a day in patients who cannot tolerate a meal. The duration of treatment depends on the severity of the disease and the patient's response. For oral candidiasis, Noxafil oral suspension is taken as 200 mg (5 ml) on the first day followed by 100 mg (2.5 ml) once a day for the following 13 days. For the prevention of invasive fungal infections, Noxafil oral suspension is given at a dose of 200 mg (5 ml) three times a day. The duration of treatment depends on the patient's condition.

For the treatment and prevention of fungal infections, the recommended dose of Noxafil tablets or Noxafil solution for infusion is 300 mg twice a day on the first day followed by 300 mg once a day thereafter; the duration of treatment depends on the severity of the disease and the patient's response. Noxafil tablets and solution for infusion must not be used for the treatment of thrush.

Patients given the solution for infusion should be switched to Noxafil tablets or oral suspension as soon as the patient's condition allows it.

For additional information, see the package leaflet.

## How does Noxafil work?

The active substance in Noxafil, posaconazole, is an antifungal medicine that belongs to the triazole group. It works by preventing the formation of ergosterol, which is an important part of fungal cell walls. Without ergosterol, the fungus dies or is prevented from spreading. The list of fungi against which Noxafil is active can be found in the summary of product characteristics (also part of the EPAR).

## How has Noxafil been studied?

In one main study, Noxafil oral suspension was studied in 238 patients with invasive fungal infections that did not respond to standard antifungal treatment. The study included 107 patients with aspergillosis, 18 patients with fusariosis, 11 with chromoblastomycosis or mycetoma, and 16 with coccidioidomycosis. The results obtained with Noxafil were compared with the records of 218 patients who were treated with other antifungal medicines. In another main study involving 350 HIV-infected patients with oropharyngeal candidiasis, Noxafil oral suspension was compared with fluconazole. In

both studies, the main measure of effectiveness was the number of patients with a complete or partial response to treatment.

The ability to prevent infections was investigated in two additional main studies, where Noxafil oral suspension was compared with fluconazole in 600 stem cell transplant patients and with fluconazole or itraconazole in 602 patients with blood or bone marrow cancer. The studies looked at the number of patients who developed an invasive fungal infection.

### **What benefit has Noxafil shown during the studies?**

In invasive aspergillosis, a successful response at the end of treatment was seen in 42% of the patients taking Noxafil oral suspension, compared with 26% of the patients in the comparator group. Noxafil also successfully treated 11 of the 18 patients who had proven or probable fusariosis, 9 of the 11 patients with chromoblastomycosis or mycetoma, and 11 of the 16 patients with coccidioidomycosis.

In oropharyngeal candidiasis, Noxafil oral suspension was as effective as fluconazole. After 14 days of treatment, both medicines had been successful in curing or improving about 92% of patients.

In the prevention studies, Noxafil oral suspension was as effective as fluconazole in stem cell transplant patients, with 5% of patients developing an infection in the Noxafil group, and 9% in the comparator group. The medicine was more effective than fluconazole or itraconazole in cancer patients, with 2% of patients developing an infection in the Noxafil group, and 8% in the comparator groups.

### **What is the risk associated with Noxafil?**

The most common side effect with Noxafil, seen in more than one patient in 10, is nausea (feeling sick). Other common side effects include vomiting, diarrhoea, pyrexia (fever) and increased bilirubin (a sign of liver problems) in the blood. For the full list of all side effects reported with Noxafil, see the package leaflet.

Noxafil must not be used in patients who are taking any of the following medicines:

- ergotamine or dihydroergotamine (used to treat migraine),
- terfenadine, astemizole (used for allergy),
- cisapride (used for stomach problems),
- pimozide (used for treating mental illness),
- quinidine (used for irregular heart beat),
- halofantrine (used to treat malaria),
- simvastatin, lovastatin or atorvastatin (used to lower cholesterol).

Caution is also needed when Noxafil is taken at the same time as other medicines. For the full list of restrictions, see the package leaflet.

## **Why has Noxafil been approved?**

The CHMP concluded that, although the first study compared Noxafil with records of patients who were actually enrolled in that study, the effectiveness of Noxafil was shown. The Committee decided that Noxafil's benefits are greater than its risks and recommended that it be given marketing authorisation.

## **What measures are being taken to ensure the safe and effective use of Noxafil?**

A risk management plan has been developed to ensure that Noxafil is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Noxafil, including the appropriate precautions to be followed by healthcare professionals and patients.

## **Other information about Noxafil**

The European Commission granted a marketing authorisation valid throughout the European Union for Noxafil on 25 October 2005.

The full EPAR for Noxafil can be found on the Agency's website: [ema.europa.eu/Find\\_medicine/Human\\_medicines/European\\_Public\\_Assessment\\_Reports](http://ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports). For more information about treatment with Noxafil, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 09-2014.